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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,185	08/07/2006	Hans-Peter Buchstaller	030863-00004	8027

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EXAMINER	
LOEWE, SUN JAE Y	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
08/20/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DCIPDocket@arentfox.com
IPMatters@arentfox.com
Patent_Mail@arentfox.com

Office Action Summary	Application No.	Applicant(s)	
	10/564,185	BUCHSTALLER ET AL.	
	Examiner	Art Unit	
	SUN JAE Y. LOEWE	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,5,9-13,15-24,28-31,34 and 35* is/are pending in the application.

4a) Of the above claim(s) *30 and 31* is/are withdrawn from consideration.

5)☒ Claim(s) *3,5,9-12,29,34 and 35* is/are allowed.

6)☒ Claim(s) *13,15-24,28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 3, 5, 9-13, 15-24, 28-31, 34 and 35 are pending in the instant application. Claims 30 and 31 remain withdrawn.

Response to Amendment

2. The amendments to the claims filed on May 7, 2009 have been fully considered. The 35 USC 112 1st paragraph and 35 USC 112 2nd paragraph rejections have been obviated and are thus hereby withdrawn.

3. Claims 3, 5, 9-11, 34 and 35 directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 11-13, 15-24, 28, 29, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on July 25, 2007 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 13, 15-24 and 28 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims
The claims are drawn to process of treating (including prophylaxis) of disorders. The claims broadly encompass any disease such as cancer, multiple sclerosis, etc.

The nature of the invention
Support is limited to the in vitro activity of the instantly claimed compounds towards RAF kinase.

The state of the prior art/level of ordinary skill/level of predictability

"Cancer" is a broad genus of diseases with extensive variability in etiology and modes of treatment. For example, different types of cancer are associated with the overexpression of different kinases. Consequently, the targeted inhibition of one family of kinases may not treat more than one type of cancer:

- Imatinib (a kinase inhibitor) is highly effective against early chronic myelogenous leukemia (CML), but less effective against blast crisis CML (Arbiser, p. 2762, published 2007)
- Sorafenib (a kinase inhibitor) was found to be relatively ineffective against melanoma (Arbiser, p. 2762)

Furthermore, state of the art for treating "cancer" via inhibition of kinases is, in general, unpredictable:

- Kinases have generally not been successful in treating advanced cancers (Arbiser, p. 2762)
- Clinical trials of tyrosine kinase inhibitors in solid tumors have been largely unsuccessful (Madhusudan et al., p. 628)
- Small molecule inhibitors of tyrosine kinases have achieved a successful transition to the clinic only in a limited number of human cancers (B. Fischer et al., p. 400, published 2007)
- Notwithstanding compelling evidence supporting a role for tyrosine kinase signaling in small cell lung cancer biology, the translation of this knowledge to the clinic has not yet been achieved (B. Fischer et al., p. 400)

The art of utilizing kinase inhibitors for the treatment of diseases outside of the scope of "cancer" appears to be nascent. However, evidence suggests a high level of unpredictability in this "nascent" art. See representative facts for multiple sclerosis (Collins, published 2007):

- It is a very difficult area to treat (p. 1750)
- Majority of compounds failed to demonstrate efficacy in clinical trials (p. 1750)
- Predicted efficacy based on preliminary studies did not result in efficacy in patient populations (p. 1750)
- T cell inhibitors were discontinued in clinical trials for failure to show efficacy in treating patient population (Table 1, p. 1747)

The amount of direction provided by the inventor/existence of working examples
No working examples are provided in the instant specification. The guidance/direction is limited to the reported in vitro activity of the instantly claimed compounds as inhibitors of protein tyrosine kinase.

The quantity of experimentation needed to make or use the invention
In the absence of working examples/direction, enablement rests on the existence of an art recognized predictable correlation between the disclosed activity and the claimed use. Evidence suggests that this requirement is not met for the instant case. Consequently,

one of ordinary skill is not enabled by the instant disclosure to practice the claimed invention. The amount of experimentation is undue.

Conclusion

4. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUN JAE Y. LOEWE whose telephone number is (571)272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sun Jae Y. Loewe/
8-12-2009

/Golam M. M. Shameem/

Primary Examiner, Art Unit 1626